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Original Article

Clinicopathological Study of 252 Jaw Bone Periapical Lesions From a Private Pathology Laboratory

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Background/Purpose: Periapical lesions are common sequelae of pulp diseases. This retrospective study evaluated the clinical and histopathological features of periapical lesions sent to a private pathology laboratory by dentists in private clinics.

Methods: Two hundred and fifty-two consecutive cases of periapical lesions were collected from September 2005 to October 2009. Clinical data and histopathological features of these periapical lesions were reviewed and analyzed.

Results: The 252 periapical lesions consisted of 128 periapical granulomas, 117 periapical cysts, and seven periapical scars. These 252 lesions were taken from 252 patients (92 men and 160 women; mean age = 43.6 years; range, 9–81 years). Of the 252 periapical lesions, 186 were found in the maxilla and 66 in the mandible. The most common site for periapical lesions was the maxillary anterior region (134 cases, including 73 granulomas, 54 cysts and 7 scars), and the most frequently involved tooth was the maxillary lateral incisor (64 cases, including 29 granulomas, 31 cysts and 4 scars). Of the 117 periapical cysts, 116 were lined by stratified squamous epithelium and one by mucoepidermoid epithelium. Hyaline bodies were discovered in the lining epithelium of four periapical cysts. Odontogenic epithelial rest, cholesterol cleft, foamy histiocytes, hemosiderin-laden macrophages, dystrophic calcification, foreign bodies, and bacterial clumps were found in five, three, nine, two, 28, 10 and one periapical granulomas, respectively, as well as in six, 11, eight, seven, 19, nine and eight periapical cysts, respectively.

Conclusion: Granulomas and cysts were the two most common periapical lesions. Periapical lesions occurred more frequently in female patients and in those in their fourth to fifth decades. The most commonly affected site for periapical lesions was the maxillary anterior region, and the most frequently involved tooth was the maxillary lateral incisor.

Key Words: periapical cyst, periapical granuloma, periapical scar

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Periapical radiolucent lesions are one of the most commonly encountered clinical findings in daily dental practice. A majority of periapical lesions are attributed to pulpo-periapical diseases and are usually managed initially by endodontic treatment. A previous study from Taiwan has shown that a total of 1,588,217 teeth were treated with non-surgical root canal treatment in 2000.[1] Within 5 years after this initial treatment, 4741 received apical surgery and 118,474 were extracted.[1] As suggested by Nair,[2] post-treatment apical periodontitis refers to the failure of complete healing of periapical alveolar bone or reduction of the apical radiolucency in root-canal-treated teeth. The etiology of post-treatment apical periodontitis can be either microbial or non-microbial. Microbial causes consist of intraradicular infection, actinomycosis and other extraradicular bacteria; whereas non-microbial causes comprise cystic apical periodontitis, cholesterol crystals, foreign bodies, and scar tissue healing.[2] In addition to radiolucency of pulpo-periapical origin, various other lesions can occur in the periapical region; these include dentigerous cyst, cementoma, periapical cemento-osseous dysplasia, periodontal diseases, traumatic bone cyst, non-radicular cyst, odontogenic keratocyst, malignant tumor, and other rarities.[3,4]

There have been inconsistent histopathological features in periapical lesions.[5–7] The incidence of cysts among periapical lesions varies greatly from 6% to 55%, and the incidence of periapical granulomas ranges from 45% to 94%.[5] These discrepancies might be due to differences in sample selection, sample size, diagnosis criteria, chronicity and size of the lesions, previous endodontic treatment, and the surgeon's preferences.[6,7] Nevertheless, an understanding of the clinical and histopathological features of periapical lesions is very important for daily dental practice.

In Taiwan, patients frequently seek treatment in private dental clinics because of convenience. In addition to general dental practitioners, a few specialists in various dental fields also provide services in private dental clinics. Whenever dental surgical specimens are obtained in private clinics, they are usually submitted to one of the private pathology laboratories for diagnosis. A retrospective analysis of the periapical lesions from the archives of a private pathology laboratory can serve to reflect the periapical disease profile of patients and daily dental practice in private dental clinics in Taiwan. The purpose of this study was to perform a retrospective analysis of the periapical lesions from a private pathology laboratory, and to investigate further the clinicopathological features of these periapical lesions.

Patients and Methods

The study group consisted of 252 cases of periapical lesions retrieved from the archives of a private pathology laboratory in Taipei, Taiwan, from September 2005 to October 2009. The tissue specimens were sent predominantly from private dental clinics and one private hospital from various regions in Taiwan. The demographic data, including the age and sex of the patients, and the affected tooth were obtained by reviewing the pathological diagnosis requisition sheets. The upper and lower jawbones were divided into three regions: the anterior (incisor/canine), premolar and molar regions. The location of the lesion was determined by the region in which the major part of the lesion was located. The dentists who performed the surgical intervention were divided into three vocational groups: (1) endodontists; (2) other dental specialists; and (3) general dental practitioners.

All surgical specimens were obtained from curettage, enucleation or extraction of the teeth with associated periapical lesions. The specimens were fixed in 10% neutral formalin for at least 24 hours, dehydrated in graded alcohol, and embedded in paraffin. The tissue blocks were cut into serial sections of 5 μm, and stained with hematoxylin and eosin. A review of the diagnosis and an analysis of the histopathological features were based on independent microscopic examination of the stained tissue sections by two oral pathologists. The sections with an inconsistent histopathological diagnosis and findings were reassessed

using a double-headed light microscope and a consensus was reached in all cases. Emphasis was placed on the type of epithelial lining of the cysts, the presence of hyaline bodies of Rushton in the lining epithelium, and the presence of odontogenic epithelial rest, cholesterol cleft, foamy histiocytes, hemosiderin-laden macrophages, dystrophic calcification, foreign bodies, and bacterial clumps in the lesions. The types of inflammation were also assessed. A mixed type of inflammation was defined as the coexistence of both acute and chronic inflammatory cells. The grade of chronic inflammation was further classified as mild, moderate and severe according to the extent of lymphoplasma cell infiltration in the tissue specimen. Mild, moderate and severe inflammation was defined if the extent of inflammatory cell infiltration was < 25%, > 25% but < 50%, and > 50% of the tissue section, respectively.

The microscopic criterion for diagnosis of a periapical cyst included the presence of an epithelium-lined cavity surrounded by a fibrous connective tissue wall. The lining epithelium was further classified into stratified squamous, mucoepidermoid (stratified squamous epithelium with scattered mucus-secreting cells), and respiratory types. A diagnosis of periapical granuloma was made if the lesion was composed mainly of fibrous or granulation tissue with various grades of acute and/or chronic inflammation. Proliferating odontogenic epithelium could be noted in cases of periapical granuloma. A periapical scar was composed of a fragment of dense fibrous connective tissue with no or minimal chronic inflammatory cell infiltration.

Results

The 252 periapical lesions consisted of 128 periapical granulomas, 117 periapical cysts, and seven periapical scars. These 252 lesions were taken from 252 patients (92 men and 160 women; mean age = 43.6 years; range, 9–81 years). The periapical lesions occurred more frequently in patients in their fourth to fifth decades, and accounted for 48.4% (122) of all patients (Table 1). The mean ages of patients with periapical granuloma, cyst and scar were 43.1, 44.3 and 43.1 years, respectively.

Table 1. Age and sex distribution of 252 patients with periapical granuloma, cyst or scar*

	Periapical granulomas ($n = 128$)	Periapical cyst ($n = 117$)	Periapical scar ($n = 7$)
Age (yr)			
0–9	0	1 (0.9)	0
10–19	4 (3.1)	6 (5.1)	0
20–29	21 (16.4)	15 (12.8)	1 (14.3)
30–39	34 (26.6)	23 (19.7)	2 (28.6)
40–49	32 (25.0)	29 (24.8)	2 (28.6)
50–59	20 (15.6)	22 (18.8)	0
60–69	7 (5.5)	16 (13.7)	2 (28.6)
70–79	9 (7.0)	4 (3.4)	0
80–89	1 (0.8)	1(0.9)	0
Sex			
Male	39 (30.5)	50 (42.7)	3 (42.9)
Female	89 (69.5)	67 (57.3)	4 (57.1)

**Data presented as n (%).*

Of the 252 periapical lesions, 186 were found in the maxilla and 66 in the mandible. The most common site for periapical lesions was the maxillary anterior region (134 cases, including 73 granulomas, 54 cysts and 7 scars), and the most frequently involved tooth was the maxillary lateral incisor (64 cases, including 29 granuloma, 31 cysts and 4 scars). Only one periapical lesion was taken from the periapical area of a primary tooth (mandibular first molar) (Table 2).

The periapical surgical interventions were mainly performed by endodontists (60.3%, 152/252), followed by other dental specialists (31.0%, 78/252), and general dental practitioners (8.7%, 22/252). Specialists other than endodontists were predominantly oral and maxillofacial surgeons who performed 76 apical surgery procedures and periodontists who performed two apical surgery procedures.

Histopathological features of 128 periapical granulomas and 117 periapical cysts are shown in Table 3. Of the 117 periapical cysts, 116 were lined by stratified squamous epithelium (Figure 1A)

Table 2. Distribution of 128 periapical granulomas, 117 periapical cysts, and seven periapical scars according to region and tooth type*

	Periapical granuloma		Periapical cyst		Periapical scar	
	Maxilla ($n=100$)	Mandible ($n=28$)	Maxilla ($n=79$)	Mandible ($n=38$)	Maxilla ($n=7$)	Mandible ($n=0$)
Regions						
Anterior	73 (73.0)	4 (14.3)	54 (68.4)	14 (36.8)	7 (100)	0
Premolar	16 (16.0)	9 (32.1)	14 (17.7)	8 (21.1)	0	0
Molar	11 (11.0)	15 (53.6)	11 (13.9)	16 (42.1)	0	0
Permanent teeth						
Central incisor	34 (34.0)	2 (7.1)	16 (20.3)	9 (23.7)	3 (42.9)	0
Lateral incisor	29 (29.0)	2 (7.1)	31 (39.2)	2 (5.3)	4 (57.1)	0
Canine	10 (10.0)	1 (3.6)	7 (8.9)	3 (7.9)	0	0
First premolar	11 (11.0)	3 (10.7)	7 (8.9)	3 (7.9)	0	0
Second premolar	5 (5.0)	5 (17.9)	7 (8.9)	5 (13.2)	0	0
First molar	9 (9.0)	12 (42.9)	9 (11.4)	9 (23.7)	0	0
Second molar	2 (2.0)	3 (10.7)	2 (2.5)	6 (15.8)	0	0
Third molar	0	0	0	0	0	0
Primary teeth						
Anterior	0	0	0	0	0	0
First molar	0	0	0	1 (2.6)	0	0
Second molar	0	0	0	0	0	0

**Data presented as n (%).*

and the remaining one by mucoepidermoid epithelium (Figures 1B and 1C). Hyaline bodies of Rushton (Figure 1D) were discovered in the lining epithelium of four periapical cysts. Odontogenic epithelial rest, cholesterol cleft (Figure 1E), foamy histiocytes (Figure 1F), hemosiderin-laden macrophages, dystrophic calcification, foreign bodies, and bacterial clumps were found in six, 11, eight, seven, 19, nine and eight periapical cysts, respectively, as well as in five, three, nine, two, 28, 10 and one periapical granulomas, respectively (Figures 2A–2F). Acute and chronic inflammation was noted in 36 periapical granulomas and 61 periapical cysts. Chronic inflammation alone was found in 92 periapical granulomas and 56 periapical cysts, with most of them showing moderate chronic inflammation (Table 3). Sulfur granules of actinomycosis were discovered in one of 117 periapical cysts (Figures 3A and 3B). All seven periapical scars were composed of dense fibrous tissue with no or minimal chronic inflammatory cell infiltration (Figure 3C).

Discussion

Our study design for evaluation of periapical lesions was similar to that performed by Bhaskar[4] and Lalonde and Leubke.[8] Bhaskar[4] studied 2308 periapical lesions from civilian endodontists and military dentists. He found that periapical granuloma (48%) was the most common type of periapical lesion, followed by periapical cysts (42%), residual cysts (3.7%), and periapical scar (2.5%). Lalonde and Leubke[8] evaluated 800 periapical lesions from 134 clinicians, including dentists form the college of dentistry, private general dental practitioners, and dental specialists (predominantly oral surgeons). They found that 45.2% of periapical lesions were periapical granulomas, 43.8% were periapical cysts, and 0.4% were periapical scars. The results of the two aforementioned studies were comparable to those of our present study. However, there existed some variations in the incidence in the other studies, which used different designs from ours.[6,7,9–11]

Table 3. Histopathological features of 128 periapical granulomas and 117 periapical cysts*

Histopathological features	Periapical granuloma ($n=128$)	Periapical cyst ($n=117$)
Lining epithelium		
Stratified squamous	0	116 (99.1)
Mucoepidermoid	0	1 (0.9)
Respiratory	0	0
Hyaline body	0	4 (3.4)
Odontogenic epithelial rest	5 (3.9)	6 (5.1)
Cholesterol cleft	3 (2.3)	11 (9.4)
Foamy histiocytes	9 (7.0)	8 (6.8)
Hemosiderin-laden macrophages	2 (1.6)	7 (6.0)
Dystrophic calcification	28 (21.9)	19 (16.2)
Foreign bodies	10 (7.8)	9 (7.7)
Bacterial clumps	1 (0.8)	8 (6.8)
Mixed acute and chronic inflammation	36 (28.1)	61 (52.1)
Chronic inflammation only		
Mild	17 (18.5)	6 (10.7)
Moderate	53 (57.6)	36 (64.3)
Severe	22 (23.9)	14 (25.0)

**Data presented as n (%).*

Mucoepidermoid lining epithelium was noted in one periapical cyst in our study. A previous hospital-based study from Taiwan demonstrated mucoepidermoid lining epithelium in three out of 377 periapical cysts.[12] The presence of mucus-secreting cells in stratified squamous lining epithelium of periapical cysts is considered to be a process of mucous metaplasia.[13] Hyaline bodies of Rushton were found in 3.4% of our periapical cysts. This incidence was comparable to that (4.5%) reported by Lin et al.[12] The origin of hyaline bodies is considered to be a secretory product of odontogenic lining epithelial cells, because these structures are usually discovered in the lining epithelium.[13]

Only one of our 117 periapical cysts was associated with a primary tooth (a mandibular first molar). This incidence (1/117) was also comparable to that (4/405) reported by Lin et al.[12] The low incidence of periapical cysts associated with deciduous dentition might be related to the common ignorance of periapical radiolucency of the primary teeth, and infections of pulpal and periapical origin in deciduous molars tend to drain more frequently than those in their permanent counterparts.[13]

The incidence of cholesterol clefts in periapical lesions has varied from 18% to 44%.[14] In the present study, cholesterol clefts were found in 5.6% (14 cases) of periapical lesions. The cholesterol crystals might come from disintegrating erythrocytes, chronic inflammatory cells or circulating plasma lipids.[5] Cholesterol clefts were always surrounded by foreign body giant cells. Nair[5] indicated that macrophages and foreign body giant cells are not able to eradicate the cholesterol deposits. It is necessary to investigate further whether these two types of phagocytic cells have a lack of enzymes to digest cholesterol, or the cholesterol crystals are too big to engulf.

Actinomycosis might be one of the etiologies for persistent periapical radiolucency or post-treatment apical periodontitis. Cases of periapical actinomycosis have been reported.[5] Stockdale and Chandler[15] also showed one case of periapical actinomycosis in 1108 periapical lesions, which was associated with a left upper lateral incisor in a 40-year-old woman. Jeansonne[16] suggested that surgical intervention to eradicate periapical actinomycosis is necessary to cure the periapical lesions. Moreover, antibiotic therapy for 6–8 weeks is mandatory for periapical actinomycosis in which infection has spread to contiguous regions.

Bacterial clumps were seen in 0.8% of specimens of periapical granuloma and 6.9% of specimens of periapical cyst in the present study. Except for actinomycosis, the presence of extraradicular infection is still controversial. Nair[5] has pointed out that microbial contamination of periapical samples might occur because microorganisms can aggregate around the apical foramen, and are easily dislodged during surgery or sampling procedures. Further studies are needed to

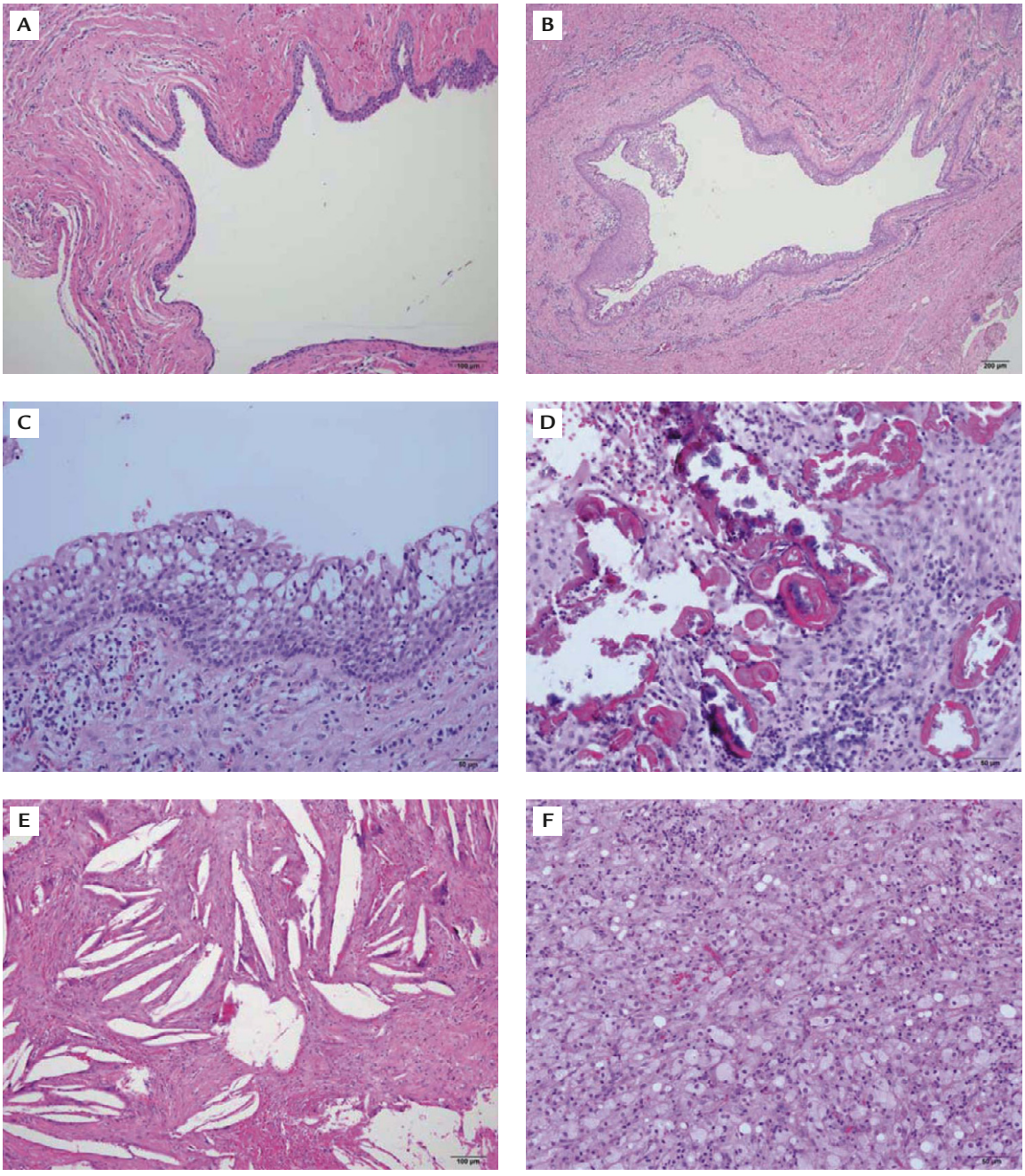

Figure 1. Histopathological features of periapical cysts. (A) A periapical cyst lined by non-keratinized stratified squamous epithelium. (B) A periapical cyst with mucoepidermoid lining epithelium. (C) High-power view of mucoepidermoid lining epithelium in (B) showing clear mucus-secreting cells in stratified squamous lining epithelium. (D) Hyaline bodies of Rushton composed of linear, curved or hairpin eosinophilic structures in the lining epithelium. (E) Cholesterol clefts with some of them being surrounded by multinucleated foreign body giant cells in the fibrous cystic wall. (F) A sheet of foamy histiocytes in the fibrous cystic wall of a radicular cyst. (Hematoxylin and eosin stain; original magnification, A and E, 10×; B–D and F, 20×).

explore the role of extraradicular microbes other than actinomyces in the pathogenesis of post-treatment apical periodontitis.

The overall incidence (7.5%) of foreign bodies in periapical lesions in the present study was higher than that (0.4%) reported by Stockdale and Chandler,[15] but lower than that (28%) reported by Love and Firth[10] and Koppang et al (31%).[17] We suggest that the majority of these foreign bodies were probably endodontic filling materials that had been pushed beyond the apical foramen during endodontic treatment procedures.

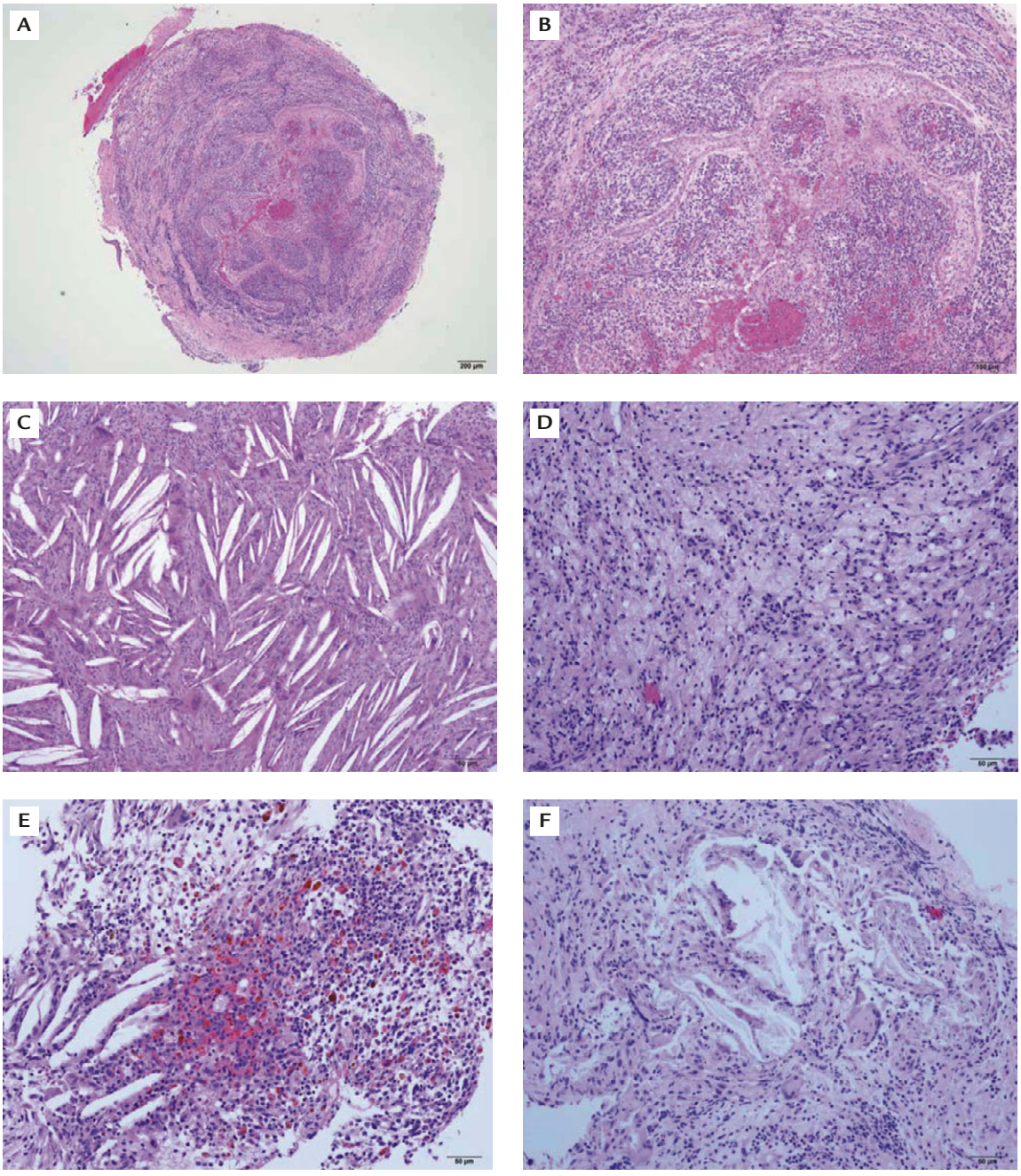

Figure 2. Histopathological features of periapical granulomas. (A) A periapical granuloma composed of granulation tissue with a severe infiltrate of chronic inflammatory cells. (B) High-power view of (A) showing proliferating odontogenic epithelium forming a network-like structure. (C) Cholesterol clefts with some of them being surrounded by multinucleated foreign body giant cells in a periapical granuloma. (D) Aggregates of foamy histiocytes in a periapical granuloma. (E) Cholesterol clefts and scattered hemosiderin-laden macrophages in a periapical granuloma. (F) Foreign bodies surrounded by multinucleated foreign body giant cells in a periapical granuloma. (Hematoxylin and eosin stain; original magnification, A, 4×; B, 10×; C–F, 20×).

Seven out of our 252 periapical lesions were diagnosed as fibrous scars. It is difficult to differentiate inflammatory periapical lesions from scar tissues by evaluation of radiographs alone. Indeed, misdiagnosis of the scar tissue as a sign of failed root canal treatment has been described in several studies.[4,10,18–20]

Hull et al[21] reported that 77.8% of apical surgery procedures were performed by endodontists, 6.6% by other dental specialists, and 15.5% by

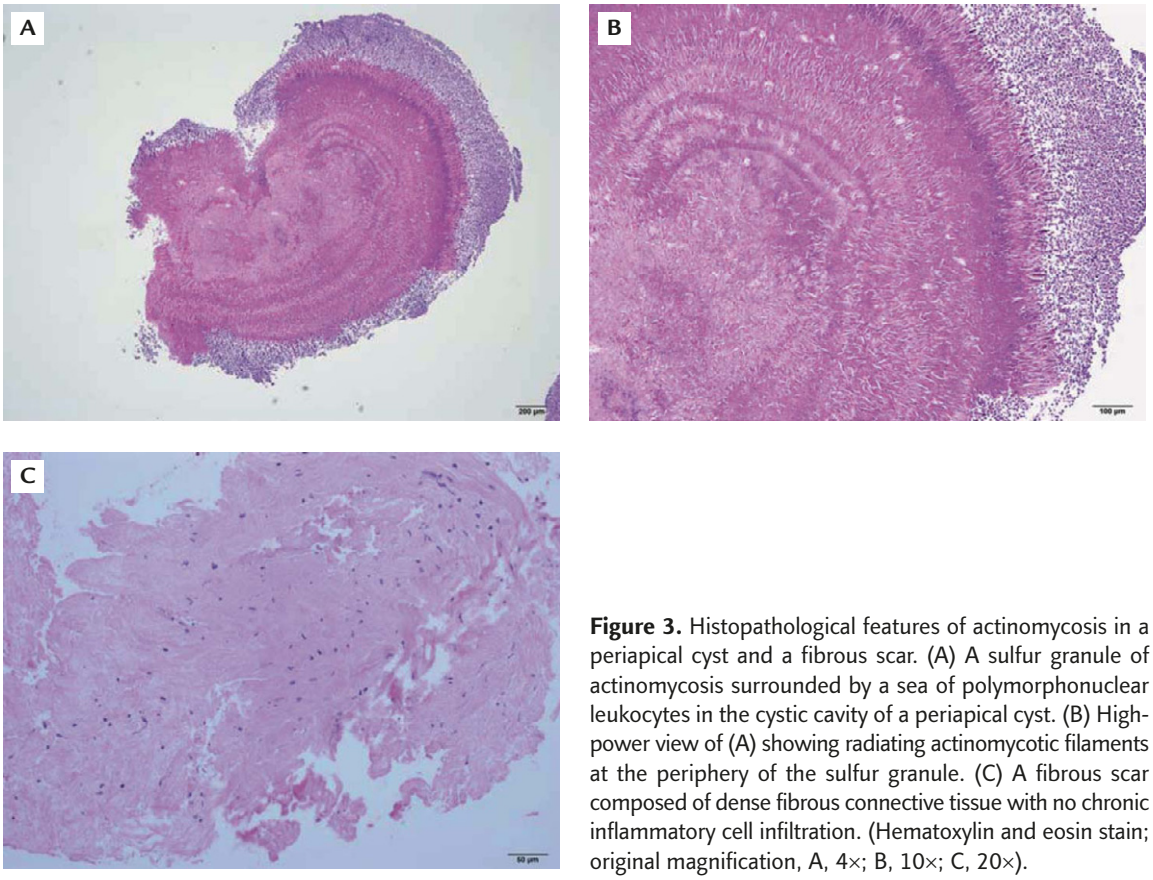

Figure 3. Histopathological features of actinomycosis in a periapical cyst and a fibrous scar. (A) A sulfur granule of actinomycosis surrounded by a sea of polymorphonuclear leukocytes in the cystic cavity of a periapical cyst. (B) High-power view of (A) showing radiating actinomycotic filaments at the periphery of the sulfur granule. (C) A fibrous scar composed of dense fibrous connective tissue with no chronic inflammatory cell infiltration. (Hematoxylin and eosin stain; original magnification, A, 4×; B, 10×; C, 20×).

general dental practitioners. In our study, the majority of apical surgery procedures were performed by endodontists (60.3%) or oral and maxillofacial surgeons (30.2%); only a minor proportion (8.7%) of procedures were carried out by general dental practitioners. These findings suggest that, in Taiwan, apical surgery procedures are restricted more to dental specialists such as endodontists and oral and maxillofacial surgeons. General dental practitioners could have a lack of apical surgery training and this forces them to refer apical surgery cases to endodontists and oral and maxillofacial surgeons.

We conclude that periapical granuloma and cysts are the two most common periapical lesions. Periapical lesions occurred more frequently in female patients and in those in their fourth to fifth decades. The most commonly affected site for periapical lesions was the maxillary anterior region, and the most frequently involved tooth was the maxillary lateral incisor.

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